

Adverse Drug Interactions in the Elderly

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Learning Objectives

- **Identify factors affecting possible drug interactions.**
- **Identify types of drug interactions.**
- **Determine criteria for identifying patients at high risk for adverse drug interactions.**
- **Identify drugs which have the greatest risk for causing the most adverse reactions in the elderly.**

Learning Objectives

- **Recognize categories of drugs used as guidance for prescribing for the elderly.**
- **Identify general guidelines for various commonly prescribed drugs.**
- **Identify dangerous drug to drug interactions.**

Potential for Adverse Drug Interactions

- On average, individuals aged 65-69 take 14 prescriptions per year
- Individuals aged 80-84 take average of 18 prescriptions per year



Potential for Adverse Drug Interactions

- **Potential for adverse drug interactions when more than one drug used:**
 - **2 drugs have 6% potential**
 - **5 drugs have 50% potential**
 - **8 drugs have 100% potential**

Inappropriate Drug Use

- **Inappropriate use of drugs estimated from 12% - 40%**
- **Estimated that for every dollar spent on drugs in nursing facilities, \$1.33 in healthcare resources spent on drug related morbidity and mortality**



Commonly Prescribed Drugs for the Elderly

- Antibiotics
- Dementia
- Psychoactive
- CV
- Hypothyroid
- DJD/arthritis
- Pain control
- Anticoagulants
- Sleep aids



Occurrence Of Drug Interactions

- **Depends on many factors**
 - **Inherent pharmacological properties of drugs**
 - **Patient's medical condition**
 - **Presence of co-morbidities**
 - **Dose of drugs**
 - **Presence of other drugs**

Identifying Major Drug Interactions

- **Which drug interactions should you worry about?**
 - **4 respected references identified 406 interactions as major**
 - **Only 9 were listed in all four references**
- **No current standard for rating drug interactions**

Which Drug Interactions Should You Worry About?

- **Some interactions very severe but uncommon**
- **Some interactions common, not life-threatening**



Which Drug Interactions Should You Worry About?

- **More concern with drugs with narrow therapeutic index**
 - **Small changes have serious consequences**
 - **Generics such as Warfarin, Digoxin, Levothyroxine, Lithium, Carbamazepine, Phenytoin, Theophylline**

Types Of Drug Interactions

- Drug – drug
- Drug – food
- Drug – disease



Identifying Patients At High Risk

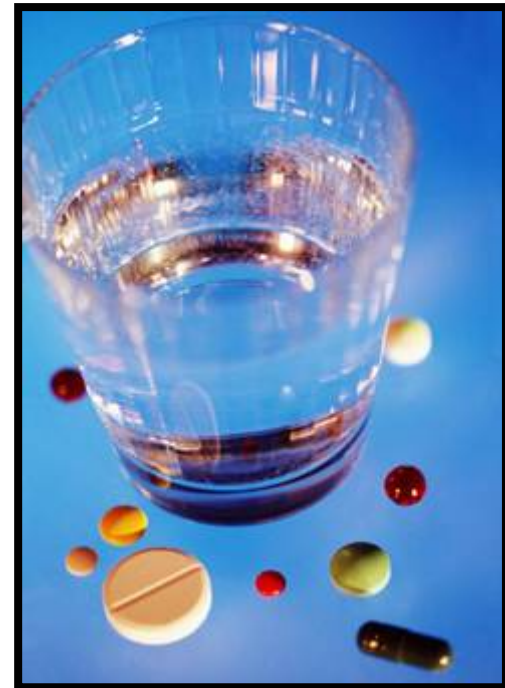
- **Medications used**
 - **Generics Digoxin, Warfarin, Lithium, Chlorpropamide**
 - **Anticonvulsants, antipsychotics, sedative/hypnotics, intermediate or long-acting benzodiazepines, narcotic analgesics, anticholinergics**

Order of Importance of Patient Risk Factors

- **>6 chronic active medical diagnoses**
- **Estimated creatinine clearance <50**
- **Low body weight**
- **Prior history of adverse drug reaction**
- **Age >85**
- **12 doses of medication per day**
- **9 medications**

Order Of Importance-Drugs with Potential for Causing Most Adverse Reactions in the Elderly

- **Anticholinergics**
- **Narcotic analgesics**
- **Digoxin [generic]**
- **Intermediate half-life benzodiazepines**
- **Antipsychotics**



Beers Criteria

- **First criteria developed by Beers and colleagues in 1991, revised in 2003, *Archives of Internal Medicine* 2003;163:2716-24**
- **Based on expert consensus**
- **Identified inappropriate use of medications in the elderly**

Beers Criteria

- **Criteria defines**
 - **Medications that should be avoided**
 - **Doses or frequencies that should not be exceeded**
 - **Medications avoided with certain disease states**
 - **Apply patients >65 years old**
 - **Identified 33 potentially inappropriate medications**

Subgroup Of Beers Criteria

- **A subsequent study later developed subgroup of Beers criteria**
- **Three tiers:**
 - **Category 1 – drugs always to be avoided**

Subgroup Of Beers Criteria (cont')

- **Category 2 – drugs rarely appropriate to use**
- **Category 3 – drugs with some indications but often used inappropriately**

Category 1

- **Drugs in Category 1: Always Avoid**
 - **Barbiturates, belladonna alkaloids and generics Flurazepam, Meprobamate, Chlorpropamide, Meperidine, Pentazocine, Trimethobenzamine, Dicyclomine, Hyoscyamine, Propantheline**

Category 2

- **Drugs in Category 2: Rarely Appropriate**
 - **Generics Chlordiazepoxide, Diazepam, Propoxyphene, Carisoprodol, Chlorzoxazone, Cyclobenzaprine, Metaxalone, Methocarbamol**

Category 3

- **Drugs in Category 3: Some Indications but often used inappropriately**
 - **Generics Amitryptiline, Doxepin, Indomethacin, Dipyridamole, Ticlopidine, Methyldopa, Reserpine, Disopyramide, Oxybutynin, Chlorpheniramine, Cyproheptadine, Diphenhydramine, Hydroxyzine, Promethazine**

Recommendations For Commonly Used Drugs

- **Iron supplements >325 mg/day**
 - **At higher doses total absorption not substantially increased, but constipation more likely**
- **Propoxyphene - avoid**
 - **Offers few analgesic advantages over acetaminophen with greater side effects**

Recommendations For Commonly Used Drugs

- **Benzodiazepines**
 - **Because of increased sensitivity, smaller doses may be as effective and safer.**

Recommendations For Commonly Used Drugs

- Total daily doses for these generics
should rarely exceed:**

Lorazepam 3 mg

Oxazepam 60 mg

Alprazolam 2 mg

Temazepam 15 mg

Zolpidem 5 mg

Triazolam 0.25 mg

Specific Considerations

- **Generics Chlordiazepoxide and Diazepam (Category 2) have long half-life in elderly (often several days). Short and intermediate-acting benzodiazepines are preferred**
- **Digoxin doses should rarely exceed 0.125 mg/day due to decreased renal clearance, except when treating atrial arrhythmias**

Specific Considerations (con't)

- **Dipyridamole [generic] (Category 2) frequently causes orthostatic hypotension in elderly and is beneficial only in patients with artificial valves**
- **Gastrointestinal antispasmodic drugs are highly anticholinergic in elderly and best avoided**

Special Considerations (con't)

- **All nonprescription and many prescription antihistamines have potent anticholinergic properties and should be avoided**
- **All barbiturates, except Phenobarbital [generic], cause excess side effects and are highly additive and should not be started as new therapy except when used to control seizures**

10 Particularly Dangerous Drug – Drug Interactions

- **Warfarin – NSAIDS**
 - **Serious GI bleeding**
 - **Consider use of COX-2 inhibitors**
 - **Caution use of Tramadol [generic] – few case reports of elevated INR**

Other Interactions

- **Warfarin – Sulfa drugs**
 - **Increased effects of Warfarin**
 - **Mechanisms possibly by decreased Vitamin K in intestinal flora**
 - **If needed, reduce Warfarin by 50% and monitor INR**

Special Considerations

- **Warfarin – Quinolones**
 - **Increased effect of Warfarin**
 - **Mechanisms possibly by decreased Vitamin K in intestinal flora**
 - **Worse with generics Ciprofloxacin, Norfloxacin, Ofloxacin, possibly Levofloxacin**

Special Considerations

- **Warfarin – Macrolides**
 - **Increased effect of Warfarin**
 - **Inhibits metabolism and clearance of Warfarin**
 - **Interaction often delayed**
 - **Monitor INR often if needed**

Special Considerations

- **Warfarin – Phenytoin**
 - **Increased effect of Warfarin and/or Phenytoin**
 - **Mechanism unknown**
 - **Obtain baseline Phenytoin and INR**
 - **Target INR towards lower end of therapeutic range**

Special Considerations

- **ACE inhibitors – potassium supplements**
 - **Elevated serum potassium**
 - **Mechanism – decreased aldosterone production and decreased potassium excretion**
 - **Monitor potassium and renal function**

Special Considerations

- **ACE Inhibitor – Spironolactone
[generic]**
 - **Elevated serum potassium**
 - **Mechanism unknown**
 - **Monitor potassium and renal function**

Special Considerations

- **Digoxin – Amiodarone [generic]**
 - **Digoxin toxicity**
 - **Mechanism: may decrease clearance of Digoxin**
 - **Obtain baseline Digoxin level, decrease dose of Digoxin by 50% and monitor levels**

Special Considerations

- **Digoxin – Verapamil [generic]**
 - **Digoxin toxicity**
 - **Synergistic effect**
 - **Monitor heart rate and EKG-PR interval**

Special Considerations

- **Theophylline – quinolones**
 - **Theophylline toxicity**
 - **Inhibition of hepatic metabolism of Theophylline by quinolones**
 - **Ciprofloxacin, Enoxacin worse.**
May use Gatifloxacin, Levofloxacin, Moxifloxacin or Trovafloxacin

Informed Consent

- **Many nursing facilities now require**
- **Informed consent for psychoactive medications**
- **Patient or legal surrogate signs if gives consent to use drugs or not**
- **Physician signature**



Case Study

An 85-year-old man with Alzheimer's is living at home with his daughter. He has been on Donepezil (5 mg) for 5 years. On Enalapril 5 mg daily for HTN. Past year has become more labile, irritable and resistant to care. Primary physician started on Risperidone 0.5mg BID. Initial improvement, but became more aggressive.

Case Study (con't)

An on-call physician prescribed Trazodone 25mg TID and increased Risperidone to 1mg BID. Patient developed unsteady gait with frequent falls. Seen by neurologist who diagnosed with Parkinsonism and started Levadopa/Carbidopa 25/100 TID.

Case Study (con't)

Became more irritable and primary physician started Lorazepam 0.5mg PRN, up to TID. Patient became more confused, sedated and combative. Appetite decreased and he stopped walking.

Case Study (con't)

Neurologist treated for depression and started Paroxetine 20mg daily and Methylphenidate 5mg BID. His confusion worsened, he stopped talking and displayed a blank stare. A head CT and laboratory workup were negative.

Case Study (con't)

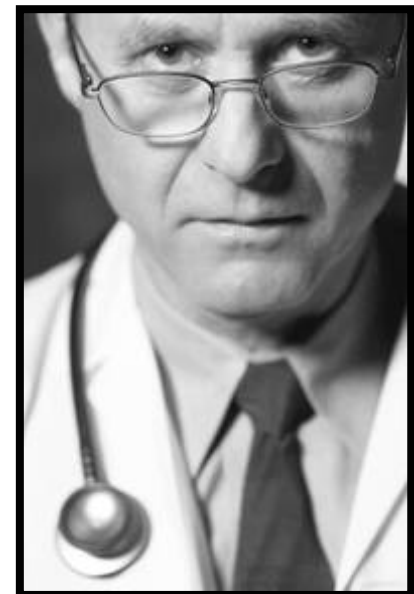
**Patient was referred to a psychiatrist.
Evaluation showed no psychotic
symptoms and scored 0/30 on MMSE.**

Case Study (con't)

Family wanted him at home and agreed to taper all medications over two weeks. By second week the confusion was better, and by six weeks he was ambulating and had a MMSE score of 18/30.

Case Discussion

- **Polypharmacy**
- **Multiple providers with no communication with each other**
- **Patient had risk factors for adverse drug reactions**



Summary

- **Factors affecting possible drug interactions**
- **Types of drug interactions**
- **Criteria for identifying patients at high risk for adverse drug interactions**
- **Drugs which have the greatest risk for causing the most adverse reactions in the elderly**

Summary

- **Categories of drugs used as guidance for prescribing for the elderly**
- **General guidelines for various commonly prescribed drugs**
- **Dangerous drug to drug interactions**